United States Senate
WASHINGTON, DC 20510

May 9, 2012

Dr. Margaret Hamburg, Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Dr. Hamburg,

We write to encourage the Food and Drug Administration (FDA) to amend its regulations to permit holders of abbreviated new drug applications (ANDAs) to initiate changes to a drug's approved labeling through the Changes Being Affected (CBE) process and Prior Approval Supplement (PAS) process.

Generic drugs are critical to consumers. Not only do they provide vital health benefits, they also save billions of dollars. With the proliferation of generic drugs, however, it is imperative to ensure that *all* prescription drugs, including generics, carry proper, accurate and up-to-date warnings about the risks they pose.

As you know, in *Pliva, Inc. v. Mensing*, 131 S. Ct. 2567 (2011), the Supreme Court held that, unlike brand name companies, generic manufacturers are not subject to states' duty-to-warn laws because FDA regulations prevent generic manufacturers from changing their labeling except to mirror the label of the brand-name, Reference Listed Drug ("RLD") manufacturer. The result is that consumers, who are injured through no fault of their own, are unable to bring failure-to-warn suits against makers of generic drugs, even though a similar suit could be brought against brand-name manufacturers.

While we believe any change must factor the importance of "sameness" in labeling between generic and brand-name products, we also believe that generics should have the ability to participate fully in the labeling process. Generics play a very large role in the market, which gives them important insights into side effects that their consumers experience. Indeed, the Supreme Court has noted that "the FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge." *Wyeth v. Levine*, 129 S. Ct. 1187, 1202 (2009).

In fact, recognizing this, the FDA already requires all drug manufacturers, including generics, to monitor, investigate and report adverse side effects experienced by users of their drug. Generic manufactures already must submit an annual report to the FDA summarizing new information that "might affect the safety, effectiveness, or labeling of the drug product." 21 C.F.R. §§ 314.81(b)(2)(i) (NDA holders) and 314.98(c)(ANDA holders). That report must include a description of actions they have "taken or intends to take as a result of this new information." *Id.* And, both a brand and generic manufacturer are subject to the requirement that their approved

"labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 C.F.R. §201.57(c)(6).

Yet, only the RLD holder can implement a strengthened warning without waiting for FDA approval through the CBE process. This process, which the FDA first adopted in 1965, is meant to ensure that new warnings about drug dangers were "placed into effect at the earliest possible time." 30 Fed. Reg. 993-94 (Jan. 31, 1965). Exactly the same reasoning justifies the adoption of a comparable policy for ANDA holders. Legislation has recently been introduced in the Senate and House that would address this important issue, but we share a belief that the FDA can and should take appropriate steps under its existing authority to effect this change.

All of us have worked to ensure that safe, affordable generic drugs are available. At the same time, we strongly urge the FDA to ensure that all drug makers, including generics, can take appropriate steps to enhance warnings given to doctors and consumers.

Sincerely,

Tom Harkin
U.S. Senator

Patrick Leahy
U.S. Senator

Al Franken
U.S. Senator